Joint Statement of the
Generic Pharmaceutical Industry Association and the National Pharmaceutical Alliance
on FDA Reform

Before the Subcommittee on Health and Environment
Committee on Commerce
April 23, 1997

Mr. Chairman and members of the Subcommittee, I am Bruce Downey, Chairman, President and CEO of Barr Laboratories, a generic drug manufacturer headquartered in Pomona, New York. I am representing the Generic Pharmaceutical Industry Association and the National Pharmaceutical Alliance. Medicines developed, manufactured and marketed by the approximately 200 members of both organizations account for more than 75 percent of all prescriptions dispensed annually in the United States.

Overview

The generic drug industry is at a critical and perplexing juncture. Unless the Congress forces the FDA to alter its budgetary priorities and provides sufficient resources for the Office of Generic Drugs, American consumers, taxpayers and providers will miss a unique opportunity to save billions of dollars in health care costs.

Generic drugs are a safe and highly cost-effective means of controlling U.S. health care costs. In 1996, American consumers spent an estimated $85.35 billion on approximately 2.41 billion drug prescriptions. Almost half of those prescriptions were filled with generics, but their cost was only about 12 percent of the total spent on prescription drugs that year. Generics typically enter the market 30 percent below the brand price and decline to 60 or 70 percent of the brand price after two years. Some generics are priced at 90 percent less than the innovator drug. Moreover, brand prices continue to rise while generic prices continue to fall. Brand product prices rose an average of 4.2 percent in 1995 and another 2.1 percent in 1996, the same year in which generic prices fell by 12.6 percent.

Thus, generic drugs provide substantial savings to taxpayers, providers and consumers, especially senior citizens, the 40 million Americans without health insurance and the underinsured.

The generic industry files over 450 applications for new generic approvals annually. Without the Herculean efforts of the dedicated staff in the Office of Generic Drugs (OGD), the generic approval process—and thus the ability to deliver lower cost, bioequivalent and therapeutically equivalent generic products—would be even more severely impaired than is currently the case. Despite their efforts, the FDA still is in serious default of its statutory requirements, and OGD is severely hampered by processes that urgently require administrative and legislative reform. For these reasons, we respectfully request that the committee address the following issues:

* allocation of consistent and adequate resources to the Office of Generic Drugs;
* pre-emption of contrary state substitution initiatives that call into question FDA's authority to determine bioequivalence and therapeutic equivalence;
* reform of the citizen petition process to ensure that market exclusivity is not unjustly extended;
* FDA must make market exclusivity decisions that comport with the act and its legislative intent; and,
* application process modernization to ensure more timely review of Abbreviated New Drug Applications (ANDAs), including implementation of binding written agreements on the design and size of appropriate bioequivalence tests.

What we hope the Subcommittee keeps in mind when considering these recommendations is that a vibrant generic pharmaceutical industry can make an enormous contribution to American health care by providing considerable opportunity for cost savings for consumers and health care providers. Moreover, by implementing these suggested reforms, Congress also has the opportunity to save literally billions of federal dollars by reducing the cost of a variety of health care programs.

For example, this year the patents of 13 drugs whose sales exceed $3.2 billion will expire. But the potential savings will be much greater in the future. Between 1997 and 2008, drugs whose current annual sales exceed $41 billion will come off patent. If the FDA was capable of fulfilling its statutory mandates on time, it could save taxpayers tens of billions of dollars over the next 12 years.

Allocation of Consistent and Adequate Resources for The Office of Generic Drugs

Unfortunately, the FDA's dedication of resources to generic drugs is inadequate to take full advantage of the unique opportunity to save billions in health care expenditures. Since 1994, the Office of Generic Drugs has suffered a decrease in over 40 FTEs, which directly contributed to the FDA's continuing inability to approve applications for generic drugs on a timely basis. For the last three years, FDA final approval time for generics has been much greater than the 180 days in which the FDA is required to review ANDAs. According to FDA's own figures, the average approval time for a generic in 1996, 1995 and 1994 was 23 months, 27 months and 24 months, respectively. Given this historical trend, OGD's resources are clearly inadequate.

Moreover, there is confusion regarding the true level of resources that the agency has committed to the Office of Generic Drugs. FDA's budgetary submission to Congress indicates that there are 327 FTE's working in the OGD. According to a senior official in this office, however, there are actually only 120 people in the office. In other words, less than 1.3 percent of the agency's 9,172 FTEs and less than 3.3 percent of its $995.9 million budget are targeted toward money-saving generic drug review and approval.

Furthermore, the proposed FY 1998 budget threatens further large cuts in the OGD. While the proposed budget of $33.5 million purports to be the same as the actual funding level for FY 97, the proposed budget includes $13 million in new, unauthorized user fees which are highly unlikely to be enacted. Unless Congress replaces these fees with appropriated monies, the Office of Generic Drugs will actually take a cut of nearly 40 percent.

The generic industry believes that any discussion of user fees should only come after the FDA is operating efficiently and in conformance with its statutory requirements for generic drug approval. To help the agency comply with its statutory mandate, we believe that the policy of diverting resources from the OGD to other, high profile but less critical functions should be reversed.

For example, in FY 96 the Offices of The Commissioner, Policy, External Affairs, and Management and Systems employed a total of 939 FTEs at a cost of $80.4 million. Moreover, using the figure of 120 persons who actually work in the OGD, there are more persons in the Office of the Commissioner or in the Office of External Affairs than in OGD. We believe that the Congress should direct the transfer of some of these less critical staff slots to reviewer positions for generic drugs, medical devices and food additives.

Ultimately, to be embraced by the generic pharmaceutical industry, any user fee proposal would have to be based on two essential assumptions. First, the OGD budget would have to be fully funded, and the FDA would have to provide services that meet all statutory requirements. Second, user fees would have to be clearly tied to some incremental improvements in timeliness of the product review and approval process, such as making available additional or higher level reviewers or statisticians for particularly complex applications. In this way, additional fees would provide clearly defined benefits for the generic industry, in the same way that PDUFA benefits the brand companies, rather than simply replacing appropriations from previous years.

Pre-Emption of Contrary State Substitution Laws

Another area that requires Congressional intervention to ensure a level playing field involves the attempt by brand companies to use state legislative and regulatory initiatives to raise marketplace barriers that preserve market share and extend exclusivity. Often, the brand companies are able to lobby for additional state or local regulation that restricts generic competition. For example, since the beginning of this year, a concerted state-by-state effort has been initiated that questions the bioequivalence and substitutability of generic versions of narrow therapeutic index (NTI) drugs. Efforts supported by brand pharmaceutical companies continue to question the bioequivalence and therapeutic equivalence of these products in state legislatures and state pharmacy board meetings.

Other brand name companies have utilized similar campaigns to prohibit the substitution of competing generics. For instance, one company sent letters to the Hawaii, Virginia and New Jersey Departments of Health objecting to the inclusion of a competing generic to the state drug formularies. Other innovator companies have asserted unsuccessfully in Illinois, New Jersey, and Florida that generic versions of their products were not therapeutically equivalent (*i.e.*, substitutable), despite FDA's contrary scientific conclusions.

Anti-generic campaigns, like those described above, are launched to unjustly preserve a product's patent and exclusivity periods beyond the time period provided for by Congress. They also undermine FDA's Congressionally-mandated drug approval process and therapeutic equivalence determinations by asserting that the generic in question is not safe, effective or therapeutically equivalent to the brand drug. By contrast, when FDA approves a generic, it determines that the drug is safe, effective and bioequivalent. The agency also determines whether that generic is "therapeutically equivalent" or "non-equivalent" to its brand counterpart. In other words, FDA decides whether the newly-approved generic has the same clinical safety and efficacy profile as that of the brand. If it does, FDA declares the generic to be a therapeutic equivalent, *i.e.*, substitutable. If not, FDA declares the product to be a therapeutic inequivalent. These agency determinations are published in FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* ("the Orange Book").

As recently as last week, the FDA reiterated that there is no basis for questioning the substitutability of NTI or other "A" rated generic medicines. In an April 16 letter to the National Association of Boards of Pharmacy, the FDA stated:

> "...in the process of evaluating applications for generic drugs, the FDA makes recommendations via a document entitled *Approved Drug Products with Therapeutic Equivalence Ratings* (the *Orange Book)* that approved multiple source drug products, including NTI drugs, are therapeutically equivalent. This term indicates that they can be substituted with the full expectation by the patient and physician that they will have the same clinical effect and safety profile as the innovator drug."

Once the FDA has determined that a generic drug is therapeutically equivalent to the innovator product, the question of substitution should be left to the doctor and patient instead of to legislators. However, despite clear scientific evidence to the contrary, legislation is pending in more than a dozen states that implies that a product determined by the FDA to be bioequivalent to a brand product is somehow inequivalent. The Congress must act aggressively to ensure that the trusted "A" rating of the FDA preempts any addition of local restrictions on substitution before the very foundation of the FDA approval process and consumer confidence in generic medicines is seriously eroded. State legislatures and various boards of pharmacy should not be in the business of developing therapeutic equivalence standards that differ from those rigorously and scientifically determined by the FDA.

Reform of the Citizen Petition Process

In addition to anti-generic state campaigns, many brand firms file citizen petitions with FDA in order to delay or foreclose the approval and dispensing of certain generics.

Because the agency must consider, by law, the merits of each citizen petition, these administrative challenges almost always result in regulatory delay—providing brand firms with months or even years of additional market dominance. The success of these challenges is not defined by whether the requested action is ultimately granted or denied but, rather, by the amount of time the generic drug is prevented from competing with the brand drug.

Past petitions have involved a myriad of scientific and public health objections, including objections to FDA's decisions on therapeutic equivalence, bioequivalence, and product characteristics. Yet, the argument common to all is that an alleged "vital" difference exists between the generic and the brand and, therefore, FDA must refrain from approving the generic product. Recent petitions have involved opposition to generic versions of conjugated estrogens, warfarin sodium, and cholestyramine powder, to name a few.

In addition to placing an unjust burden on consumers who would benefit from the availability of lower cost, equivalent therapies, the citizen petition process burdens the already constrained resources of the FDA and OGD. According to the Office of Generic Drugs, a substantial percentage of senior staff time is diverted to reviewing the 32 citizen petitions that are currently pending at OGD. Without reform of this process, the FDA will be faced with an increasing number of similar attempts to extend market exclusivity.

One way to reform this process is to require the filers of such petitions to demonstrate through “substantial scientific proof” that their proposed changes are necessary to ensure patient safety. In addition, we propose that the simple act of filing a petition could not offset any pending application unless the data filed conclusively demonstrated that a health and safety risk was present.

Application Process Modernization

The drug approval process, whether for a brand or a generic product, is complex and lengthy. In addition, it carries the extraordinary burden of ensuring patient safety.

Therefore, discussion of approval times and the unpredictable nature of the approval process should not be confused with any intention to sacrifice safety for speed. That said, the generic industry believes that there are numerous and significant opportunities to modernize the FDA approval process, eliminate duplication, expedite the process and enhance the approval mechanism. In cooperative discussions with FDA, the industry has examined a number of these options. OGD and FDA have embraced many, including implementing electronic data filing, streamlining labeling procedures and increasing the quality and quantity of informal communications in an effort to resolve questions and make the complex approval process less confusing and more timely.

One area that must be addressed by Congress, however, involves the need for binding bioequivalence determinations. Currently, standards for approval can be modified throughout the approval process, in effect changing the rules for the generic pharmaceutical company well after the game has started. To rectify this fluid approval process, the industry proposes that bioequivalence protocols submitted to the Agency must be approved in writing within a set period of time—30 days for example—after which there could not be changed except for compelling safety reasons as opposed to the whim of the reviewer.

FDA Must Make Market Exclusivity Decisions
That Comport With The Act And Its Legislative Intent

For over 10 years, FDA has maintained well-established market exclusivity positions. Historically, the agency has interpreted the market exclusivity provisions of the Act narrowly. Specifically, the agency has consistently granted 5 years of market exclusivity for new chemical entities, thereby denying exclusivity to enantiomers of previously approved racemate drug products. Recently, however, FDA has considered reversing this well-grounded position.

To briefly explain, a "racemate" is a chemical compound made up of two enantiomers with 50:50 proportions. The two enantiomers are molecules that are mirror images of each other, yet differ in the spatial orientation of the atoms. It is a "known and predictable" fact that the therapeutic value of a drug "lie[s] either in the racemate or in only one of its two isomers." It is, therefore, no surprise when a firm establishes that one enantiomer of a racemate holds the therapeutic usefulness of the product. Because the Act awards 5 years of exclusivity for new active moieties, the agency has held that enantiomers of previously approved racemates are not eligible for 5 years of market exclusivity. Simply put, because each enantiomer was approved in the original racemate product, an award of 5 years of exclusivity is not appropriate.

We maintain that the statute's plain meaning and legislative history support FDA's current interpretation. More importantly, however, an agency reversal of this policy would deter good science and chill market competition. Specifically, a policy reversal would provide brand firms with an incentive to develop racemate products first, regardless of whether the firm knows or suspects that a single enantiomer product would be clinically superior. Yet, good science is advanced only by encouraging manufacturers to initially market the best product for the therapeutic condition of use. Under the agency's proposed policy, firms may be inclined to neglect the development of new products that represent significant clinical advancement, in favor of a second generation enantiomer product that treats the same condition of use as the parent racemate. Thus, a reversal of agency policy may harm pharmaceutical innovation rather than encourage it.

FDA's proposed policy reversal also would frustrate the Act's objective of fostering pharmaceutical competition. Specifically, the reversal would permit brand firms to receive possibly 15 consecutive years of market exclusivity—5 years for the racemate, followed by 5 years for each enantiomer of the racemate—a lengthy exclusivity period not contemplated by the Act. Thus, under that scenario, brand firms would receive an enormous and unjustified economic windfall without producing an innovative product.

In addition to 5 years of market exclusivity for new chemical entities, the Act also provides 3 years of market exclusivity for new products representing significant innovation, when supported by new clinical studies essential to the product's approval. Despite the clear language of the Act, the agency has recently awarded 3 years of market exclusivity for simply switching a product's status from prescription (Rx) to over-thecounter (OTC). Market exclusivity has been granted to OTC products even though the products did not represent significant innovation. Instead, the intended use, dosage form, dosing schedule, and route of administration were identical for both the Rx and the OTC product versions. Moreover, these applications were not supported by clinical studies essential to the product's approval but, rather, by market surveys on OTC use and label comprehension studies. This agency decision contravened the Act and its legislative history, which provide that market exclusivity is intended as an incentive for developing new drugs, and is not to be granted for a minor change or variation of a previously approved drug.

In sum, the agency should not be permitted to interpret the Act to grant exclusivity periods for minimal research and development efforts. Congress should prevent these actions by amending the Act to clarify its market exclusivity position. Specifically, market exclusivity should be awarded only if the applicant has conducted adequate, well-controlled, double-blind studies that are essential to the approval of a product, and where that product represents a substantial innovative change.

Congress Should Adopt a Legislative Process to Ensure that Consideration of Patent Extensions are Conducted in the Open

In the last Congress, a number of specific patent extensions were attempted through a variety of legislative vehicles, nearly all of which bypassed the normal process of review by the committees of primary jurisdiction. For example, as recently reported in *U.S. News & World Report,* last spring an amendment was slipped into a budget bill at the last minute that extended the patent of Searle's anti-inflammatory drug Daypro®. The amendment allowed Searle to sell Daypro®, which has annual sales of approximately $280 million, for two more years without generic competition.

Similar attempts were made to extend the patent exclusivity of Lodine®, Claritin®, and Relafen®, whose combined annual sales far exceeded $1 billion. These attempts were unsuccessful despite a massive lobbying campaign by certain brand companies in the last Congress, but new efforts have already surfaced to put patent extensions for Claritin® and Toradol®, a Roche Laboratories Inc. drug, in the supplemental appropriations bill now working its way through the legislative process.

Obviously, these *ad hoc* patent extension efforts disrupt the efforts of committees like Appropriations and Armed Services which are struggling to resolve difficult legislative issues within their normal jurisdiction. These end run tactics also prevent open debate on the proposed extensions, and result in accusations by the media and public interest groups that Congress is willing to circumvent the normal legislative process when pressured by brand name companies.

To prevent this from constantly recurring, we propose that Congress create a process to provide for the fair and open review of specific patent extension proposals. This could be modeled after the process that private relief legislation is required to undergo. Under this procedure, each proposed patent extension bill would be referred to a specific committee, such as the Senate and House Judiciary Committees, where the proposed extension would have to be debated and reviewed on its merits. Hearings could be held and the arguments of all interested parties could be weighed by the committee or by an independent entity, such as the General Accounting Office. Most important, such a process would ensure that a request for a patent extension was judged on its merits and remove any perception that lobbying influence or campaign contributions by the innovator were the determining factor.

Conclusion

In summary, the GPIA and the NPA believe that the contribution of the generic industry to controlling consumer and health care costs could be significantly enhanced by adopting actions such as those listed above. Adequate funding of the Office of Generic Drugs; federal pre-emption of state attempts to usurp the authority of the FDA regarding therapeutic equivalence and substitution; modification of the citizen petition process to eliminate “gaming the regulatory system;” market exclusivity decisions that comport with the act and its legislative intent; and, modernization of the approval process including the adoption of written bioequivalence protocols, could significantly strengthen the industry to the benefit of all consumers, taxpayers, and health care providers. We look forward to an opportunity to discuss these issues with the Committee in greater detail.